

In the Claims

Claims 1-62 (canceled)

63. (New) An implantable construct suitable for implantation into a cartilage lesion or defect, said construct prepared by a process of converting isolated non-active, non-dividing, mature chondrocytes that are not able to produce extracellular matrix macromolecules into rejuvenated metabolically and genetically activated chondrocytes that are able to divide, multiply and synthesize the extracellular matrix macromolecules, said process comprising steps:

- a) isolating chondrocytes from a donor's joint cartilage;
- b) expanding said isolated chondrocytes of step a) by culturing said chondrocytes in a culture medium;
- c) suspending the cultured chondrocytes of step b) in a collagen containing solution, gel or thermo-reversible hydrogel;
- d) introducing said suspension of step c) into a collagenous support matrix thereby seeding said matrix with suspended chondrocytes; and
- e) subjecting said chondrocytes seeded within said support matrix of step d) to an activation step for from about one week to about three months, said activation step comprising applying to said support matrix seeded with chondrocytes a cyclic hydrostatic pressure from about 0.01 MPa to about 10 MPa above atmospheric pressure, said pressure being applied at a frequency of from about

0.01 to about 2 Hz, for from about one hour to about 30 days, followed by a resting period from about one day to about sixty days, said activation step further performed under perfusion with a perfusion medium at a flow rate from about 1 to about 500  $\mu$ L per minute, wherein during said activating step said inactive non-dividing chondrocytes seeded within said support matrix are activated to divide, multiply and to synthesize said extracellular matrix macromolecules thereby forming said implantable construct;

wherein said chondrocytes of step a) are mature, inactive and non-dividing chondrocytes unable, without employing the activation step e) to synthesize the extracellular matrix macromolecules and wherein said chondrocytes are isolated from a donor's joint cartilage by enzymatic digestion;

wherein said collagenous support matrix of step d) is a collagenous sponge, collagenous scaffold, collagenous honeycomb or collagenous honeycomb-like lattice, each containing a plurality of pores having a size ranging from about 50  $\mu$ m to about 500  $\mu$ m;

wherein said formed implantable construct comprises more than 5% of activated chondrocytes and a ratio of the newly synthesized extracellular matrix to activated chondrocytes is lower than 95:5.

64. (New) The construct of claim 63 wherein said collagenous support matrix is prepared from a material selected from the group consisting of a Type I collagen; Type II collagen; Type IV

collagen; a collagen containing glycosaminoglycan, agarose or hyaluronin; a collagen containing proteoglycan, glycoprotein, gelatin, fibronectin, laminin, bioactive peptide, growth factor or cytokine; a collagen containing a synthetic polymeric fiber made of a polylactic acid, polyglycolic acid, polyamino acid or polycaprolactone; and a combination thereof.

65. (New) The construct of claim 64 wherein said support matrix is prepared from the Type I collagen.

66. (New) The construct of claim 65 wherein said applied cyclic hydrostatic pressure is from about 0.5 MPa to about 5 MPa applied at a frequency of about 0.5 Hz for from about seven to about fourteen days followed by the resting period from about seven to about twenty-eight days.

67. (New) The construct of claim 66 wherein said applied hydrostatic pressure is about 3 MPa applied at a frequency of about 0.5 Hz.

68. (New) the construct of claim 67 wherein said perfusion flow rate is from about 5 to about 50  $\mu$ L per minute.

69. (New) The construct of claim 68 wherein said perfusion rate is about 5  $\mu$ l/min.

70. (New) The construct of claim 63 wherein said activation of the chondrocytes of step e) is additionally performed under a reduced oxygen concentration of less than 20%.

71. (New) The construct of claim 70 wherein additionally said activation of chondrocytes is performed at about 5% concentration of carbon dioxide.

72. (New) The construct of claim 63 wherein said support matrix has pores from about 100  $\mu$ m to about 300  $\mu$ m.

73. (New) The construct of claim 72 wherein said support matrix has pores from about 200  $\mu$ m.

74. (New) The construct of claim 63 wherein said perfusion rate is from about 5  $\mu$ l/min to about 50  $\mu$ l/min.

76. (New) The construct of claim 63 wherein said isolated chondrocytes of step a) are autologous.

77. (New) The construct of claim 63 wherein said support matrix is the collagenous sponge or collagenous honeycomb seeded with isolated and expanded chondrocytes suspended in the Type I collagen solution.

78. (New) An implantable construct suitable for implantation into a cartilage lesion or defect, said construct prepared by a process of converting isolated non-active, non-dividing, mature chondrocytes that are not able to produce extracellular matrix macromolecules into rejuvenated metabolically and genetically activated chondrocytes that are able to divide, multiply and synthesize the extracellular matrix macromolecules, said process comprising steps:

- a) isolating chondrocytes from a donor's joint cartilage;
- b) expanding said isolated chondrocytes of step a) by culturing said chondrocytes for about 3 to about 28 days in a culture medium;
- c) suspending the cultured chondrocytes of step b) in a collagen containing solution, gel or thermo-reversible hydrogel;
- d) seeding a collagenous support matrix with a chondrocyte suspension of step c); and
- e) subjecting said chondrocytes seeded within said support matrix of step d) to an activation step for from about one week to about three months, said activation step comprising applying to

said support matrix seeded with chondrocytes a cyclic hydrostatic pressure from about 0.5 MPa to about 5 MPa above atmospheric pressure, said pressure being applied at a frequency of about 0.5 Hz, for from about five to about ten days, followed by a resting period from about ten to about fourteen days, said activation step further performed under perfusion with a perfusion medium at a flow rate from about 5 to about 50  $\mu$ L per minute, wherein during said activating step said inactive non-dividing chondrocytes seeded within said support matrix are activated to divide, multiply and to synthesize a new extracellular matrix macromolecules thereby forming said implantable construct;

wherein said chondrocytes of step a) are mature, inactive and non-dividing chondrocytes unable, without employing the activation step e) to synthesize the extracellular matrix macromolecules, wherein said chondrocytes are isolated from a donor's joint cartilage by enzymatic digestion;

wherein said collagenous support matrix of step d) is a collagenous sponge, collagenous scaffold, collagenous honeycomb or collagenous honeycomb-like lattice, each containing a plurality of pores having a size ranging from about 50  $\mu$ m to about 500  $\mu$ m;

wherein said formed implantable construct comprises more than 5% of activated chondrocytes and a ratio of the newly synthesized extracellular matrix to activated chondrocytes is lower than 95:5.

79. (New) The construct of claim 78 wherein said collagenous support matrix is prepared from a material selected from the group consisting of a Type I collagen, Type II collagen, Type IV collagen and a combination thereof.

80. (New) The construct of claim 79 wherein said support matrix is prepared from the Type I collagen.

81. (New) The construct of claim 80 wherein said applied cyclic hydrostatic pressure is about 3 MPa applied at a frequency of about 0.5 Hz.

82. (New) The construct of claim 81 wherein said activation step is performed at oxygen concentration from about 1 and about 20%.